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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,470	03/11/2004	Daniel H. Teitelbaum	UM-08764	7421

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,470	TEITELBAUM ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7 and 18-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7, 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Request for Continued Examination (RCE) filed October 25, 2006, along with the required fee under 37 CFR 1.114, is acknowledged and accepted. New claims 22 and 23 are presented. Accordingly, claims 1-5, 7 and 18-23 are now under consideration.

Claims 18 and 21 were rejected under 35 U.S.C. 112, second paragraph, in the last Office Action as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. It was asserted there is insufficient antecedent basis for the limitation "colitis" in independent claim 1 from which claims 18 and 21 depend.

The rejection of record under 35 U.S.C. 112, second paragraph, is withdrawn following amendments to the claims. The various parameters disclosed on page 20 of the specification show the means to ascertain improvement in inflammatory bowel disease in a laboratory model of inflammatory bowel disease, i.e., inflammation of the colon.

In the last Office Action claim 20 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Subsequent to the deletion of "prevents" in claim 20, the rejection of record under 35 U.S.C. 112, first paragraph, is withdrawn.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22 and 23 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In the instant case, the claims recite the limitation "wherein reduction of inflammatory bowel disease in said subject is detectable by an improved histologic colitis score of said subject" and "wherein reduction of severity of inflammatory bowel disease in said subject is detectable by the absence of the loss of body weight in said subject", respectively. There is insufficient written description for application of these parameters for ascertaining improvement to subjects having short bowel syndrome. This is a Written Description rejection.

> M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

While the specification describes the administration of the ACE inhibitor enalaprilat in a mice colitis model on page 20, and improvement is demonstrated, it does not describe improvement in a model depicting short bowel syndrome.

On page 4 of the specification, the compositions of the invention are stated to be administered to infants, children, and adults who suffer from short bowel syndrome, a

condition in which the subject is lacking a sufficient length of the gastrointestinal tract to permit the normal absorption of fluids, electrolytes and nutrients to permit growth and survival. The use of angiotensin converting enzyme inhibitors is said to facilitate growth and adaptation of the gastrointestinal tract. No nexus to short bowel syndrome is apparent from Table 1 on page 20 of the specification. Thus, the disclosure lacks sufficient written description for methods of treating short bowel syndrome comprising administering an angiotensin converting enzyme inhibitor "wherein reduction of inflammatory bowel disease in said subject is detectable by an improved histologic colitis score of said subject" and "wherein reduction of severity of inflammatory bowel disease is said subject is detectable by the absence of the loss of body weight in said subject", respectively, are shown.

Claims 1-5, 7 and 18-21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Rodgers et al., U.S. Patent 6,821,953, which is not an anticipatory reference, in view of The Merck Index, in the last Office Action. It was asserted Rodgers teaches the administration of angiotensin converting enzyme (ACE) inhibitors along with a peptide fragment in various inflammatory conditions of the bowel, such as ulcerative colitis. See claim 11, as well as column 3, lines 4-25, where examples of angiotensin converting enzyme inhibitors are disclosed. Further, the **Inflammatory Bowel Diseases** section of the The Merck Index establishes that weight loss, histological parameters, heme positive stools and clinical symptoms are routinely followed in patients having inflammatory bowel diseases.

Applicants argue Rodgers does not provide any type of administration protocol nor examples demonstrating the use of an ACE inhibitor in the treatment of inflammatory bowel disease or short bowel syndrome.

Applicants' arguments have been given careful consideration but are not found persuasive. The rejection of record of claims 1-5, 7 and 18-21 under 35 U.S.C. 103(a) as being unpatentable over Rodgers et al., U.S. Patent 6,821,953, in view of The Merck Index, is maintained, and presently extended to include new claims 22 and 23.

The open language of the present claims allows for the inclusion of any number of additional active agents in the claimed methods. A reduction in the characteristics that define an inflammatory bowel disease, such as histological parameters, the presence of heme positive stools, weight loss and clinical severity of colitis are taught by the Merck Index and the qualitative and quantitative determinations of such characteristics are conventionally examined when a practitioner skilled in the art of gastroenterology ascertains the progression of an inflammatory bowel disease. The determination of optimal modes of administration are parameters that are well within the purview of those skilled in the art through no more than routine experimentation. Thus the teachings of the prior art suggest the claimed subject matter to a person of ordinary skill in the gastroenterology art and reveal a reasonable expectation of success.

In the last Office Action claims 1-5 and 18-21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Acton et al., U.S. Patent 6,632,830, in view of The Merck Index. It was asserted Acton teaches the administration of an angiotensin converting enzyme (ACE) inhibitor in the treatment of an inflammatory bowel disease. See column 36, lines 60- 61, as well as column 37, lines 12-23, and columns 41-43, where modes of administration are disclosed. Further, the **Inflammatory Bowel Diseases** section of the The Merck Index establishes that

weight loss, histological parameters, heme positive stools and clinical symptoms are routinely followed in patients having inflammatory bowel diseases.

Applicants argue Acton does not provide any particular examples of inflammatory bowel diseases that might benefit from administration of an ACE-2 inhibitor or any specific administration protocol for how to use an ACE-2 inhibitor to treat an inflammatory bowel disease. Further, Applicants urge Acton fails to provide any examples demonstrating the use of an ACE-2 inhibitor in the treatment of inflammatory bowel disease or short bowl syndrome.

Applicants' arguments have been given careful consideration but are not found persuasive. The rejection of record of claims 1-5 and 18-21 under 35 U.S.C. 103(a) as being unpatentable over Acton et al., U.S. Patent 6,632,830, in view of The Merck Index, is maintained and presently extended to include claim 7 and new claims 22 and 23. See column 2, lines 62-64, where, as required by instant claim 7, captopril, enalapril, fosinopril, linsinopril and ramipril are depicted as examples of those ACE inhibitors contemplated by Acton.

A reduction in the characteristics that define an inflammatory bowel disease, such as histological parameters, the presence of heme positive stools, weight loss and clinical severity of colitis are taught by the Merck Index and the qualitative and quantitative determinations of such characteristics are conventionally examined when a practitioner skilled in the art of gastroenterology ascertains the progression of an inflammatory bowel disease. The determination of optimal modes of administration are parameters that are well within the purview of those skilled in the art through no more than routine experimentation. Thus the teachings of the prior art suggest the claimed subject matter to a person of ordinary skill in the gastroenterology art and reveal a reasonable expectation of success.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

January 2, 2006 Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER